14. (AMENDED) The polynucleotide according to Claim 13, wherein the autoproteolytic peptide is fused to the N-terminus of the viral protein, wherein the protein of interest is fused to the N-terminus of the autoproteolytic peptide.

A2 cont

15. (") The polynucleotide according to Claim 1, wherein the protein of interest is a plant protein.

16. The polynucleotide according to Claim 15, wherein the plant protein is a structural protein, enzyme, or a protein involved with pigmentation.

A3

21. The polynucleotide according to Claim 1, wherein the fusion protein can be expressed in a plant or a plant cell.

A4

25. The plant cell according to Claim 24 wherein the plant cell is a monocot plant cell.

A5

27. The plant according to Claim 26 wherein the plant is a monocot plant.

A6

58. (") A viral genome comprising at least one duplicated genomic nucleic acid component, wherein the duplicated genomic nucleic acid component encodes a promoter operatively linked to a fusion protein, wherein the promoter is functional in a plant or plant cell and is native to the virus, and wherein the fusion protein comprises (1) a viral protein, (2) a protein of interest wherein the protein of interest is non-native to the viral genome, and (3) an autoproteolytic peptide, wherein (3) is fused between (1) and (2).

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record. In accordance with the requirements of 37 C.F.R. § 1.121, a marked up version showing the changes to the claims, is attached herewith as Appendix A. For the Examiner's convenience, a complete claim set of the currently pending claims is also submitted herewith as Appendix B.

REMARKS

Status of the Claims.

Claims 1-30 and 58 are pending with entry of this amendment. Claims 31-57 and 59-67 have been cancelled; cancellation of these claims is without prejudice, without intent to abandon any originally-claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications containing these cancelled claims.

Claims 1-16, 21, 25, 27 and 58 have been amended. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record. No new matter has been added to the application by way of the above amendments. With respect to claim 1 and 58, support for the promoter functional in a plant or plant cell can be found throughout the specification at, for example, page 14, lines 29-30; and page 28, line 1 through page 29, line 5; support for the autoproteolytic peptide comprising no more than 20 amino acids can be found at, for example, page 13, line 33 through page 14, line 1. With respect to claim 7, support for the 2A autoproteolytic peptide from foot and mouth disease can be found throughout the specification at, for example, page 13, lines 11-16. The remaining amendments address typographical errors and informalities; no new matter has been entered by way of these amendments which are entirely formal in nature.

Election/Restriction.

Pursuant to a restriction requirement made final, Applicants cancel claims 31-57 and 59-67 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter, and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statement (Form 1449) submitted on May 21, 2001.

35 U.S.C. §101

Claims 1-14, 17, 19, 21-23, 28-30 and 58 were rejected under 35 USC §101 as allegedly being directed to non-statutory subject matter. Applicants traverse.

The cited claims (as amended) are drawn to polynucleotides encoding a promoter operatively linked to a transcriptional unit, wherein the promoter comprises a promoter functional in a plant or plant cell, and wherein the transcription unit encodes a fusion protein, wherein the fusion protein comprises (1) a viral protein, (2) a protein of interest, and (3) an autoproteolytic peptide comprising no more than 20 amino acids, wherein (3) is fused between (1) and (2). The foot and mouth disease virus is an animal virus, and as such does not contain a promoter functional in a plant or plant cell. Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §112, Second Paragraph

Claims 7, 10, 13, 14, 17 and 58 were rejected under 35 U.S.C. §112, second paragraph, as lacking antecedent basis or as indefinite because the metes an bounds are allegedly undefined. Applicants traverse to the extent that the rejections apply to the amended claims.

Claim 7 was rejected as allegedly indefinite in use of the phrase "2A autoproteolytic peptide." Applicants have amended the claim to more clearly cite "a 2A autoproteolytic peptide from a foot and mouth disease virus" and respectfully request that the rejection be withdrawn.

Claims 10 and 13 were rejected as allegedly indefinite with respect to the shorthand terms "γb" and "βb", respectively. Although not specifically noted, claims 14 and 17 were presumably rejected for being dependent upon rejected claim 13. Applicants submit that these abbreviations are commonly used by one of skill in the art of virology, particularly with respect to RNA type viruses having multiple RNA genomic components (e.g. RNA-α, RNA-β and RNA-γ). The nomenclature clearly indicated the coding position of the protein (for example: a, b, or c) as well as the RNA genome from which it is derived (α, β or γ). As such, Applicants submit that the terms are not indefinite for failing to particularly point out and distinctly claim which protein is referenced or from were it comes; such information is inherent in the name itself and readily understood by one of skill in the art of RNA viruses. Applicants respectfully request that the rejection be withdrawn.

Claim 58 has been amended to clarify the issue of antecedent basis, as helpfully pointed out by the Examiner. In light of the amendment, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §112, First Paragraph

Claims 7, 10, 13, 14 and 17-20 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification. Applicants traverse to the extent that the rejection applies to the amended claims.

Claim 7 was rejected based upon the phrase "2A autoproteolytic peptide." The term "autoproteolytic peptide" is defined in the specification at page 13, lines 11-14, as "any amino acid sequence that can essentially independently cleave itself by breaking a peptide bond or covalent bond with its sequence in the presence of heterologous amino acid sequences at both its N- and C-terminal ends." One example as provided in the specification is the 2A peptide of the foot and mouth disease virus. As such, the subject matter has been described in the specification on such a

way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention at the time the application was filed. However, in the interest of furthering prosecution, Applicants have amended the claim to more clearly cite "a 2A autoproteolytic peptide from a foot and mouth disease virus" and respectfully request that the rejection be withdrawn.

Claims 10 and 13 were rejected based upon the terms "γb" and "βb", respectively. Claims 14 and 17-20 were presumably rejected for being dependent upon rejected claim 13. Applicants submit that these abbreviations are defined in the specification, and are commonly used by one of skill in the art of virology, particularly with respect to RNA type viruses as noted above. As provided in the specification at page 24, lines 19-20, the term βb refers to an RNA-β encoded 60kDa disease specific protein having a nucleotide binding motif similar to an RNA-α encoded protein (αa). The term γb refers to an RBA-γ encoded 17 kDa cysteine rich protein (page 24, lines 29-30). Since the claimed subject matter is described in the specification, Applicants submit that the rejection is improper and respectfully request that the rejection be withdrawn.

35 U.S.C. §102

Claims 1, 2, 7 and 11 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Donnelly et al. (1997 Journal of General Virology 78:13-21). Applicants traverse.

To establish a *prima facie* case of anticipation, the Office must establish how the references at issue anticipate each element of the rejected claims. Claim 1 as amended is drawn to a polynucleotide encoding a promoter operatively linked to a transcriptional unit, wherein the promoter comprises a promoter functional in a plant or plant cell, and wherein the transcription unit encodes a fusion protein, wherein the fusion protein comprises (1) a viral protein, (2) a protein of interest, and (3) an autoproteolytic peptide comprising no more than 20 amino acids, wherein (3) is fused between (1) and (2)

The cited art does not teach the limitations of the claimed invention. Donnelly is alleged to teach a polynucleotide encoding a promoter operatively linked to a transcription unit as described in the present invention. In addition, Donnelly is alleged to teach a viral protein from an RNA virus and a 2A autoproteolytic peptide at page 16, legend of Figure 2. However, the plasmids used in Donnelly are T7-based sequences (see Figure 2), which are then cloned into pUC8 and used to transform *E. coli* (2nd paragraph on page 17; 2nd full paragraph on page 18). These constructs

are designed for prokaryotic expression, and as such do not contain promoters that are functional in a plant or plant cell.

The Office Action does not provide how Donnelly teaches or discloses a promoter functional in a plant or plant cell. Furthermore, the Office has noted that Donnelly does not teach plant viruses or monocot plants (paragraph 11 of the Office Action). Since the cited art does not teach the limitations of the claimed invention, Applicants respectfully request that the rejection be withdrawn.

Although not an issue with respect to anticipation, claims 1, 2, 7 and 11 are also not obvious over Donnelly. Claim 1 recites in part "wherein the promoter comprises a promoter functional in a plant or plant cell". The Office Action correctly states that Donnelly does not teach plant viruses or monocot plants; rather, Donnelly is directed towards animal virus sequences disposed within plasmids for expression in prokaryotes. As such, polynucleotides with promoters functional in plant cells are not considered. It would not be obvious to substitute the animal viral sequence of Donnelly having a promoter that is expressible in a prokaryote with the promoter of the present invention that is expressible in a plant cell.

35 U.S.C. §103(a).

Claims 1-4, 7, 9-12, 15, 16, 19, 20 and 24-27 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Donnelly in view of Choi et al. (2000 Plant Journal 23:547-555). Applicants traverse.

Three requirements must be met for a *prima facie* case of obviousness. First the prior art reference(s) must teach all of the limitations of the claims. M.P.E.P. § 2143.03. Second, there must be a motivation to modify the reference(s) or combine the teachings to produce the claimed invention. M.P.E.P. § 2143.01. Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. The teaching or suggestion to combine and the expectation of success must both be found in the prior art and *not based on Applicant's disclosure.* M.P.E.P. § 2143.

The rejection does not establish how the cited art teaches the claims of the present invention. Claims 1-4, 7, 9-12, 15 and 16 are drawn to a polynucleotide encoding a promoter operatively linked to a transcriptional unit, wherein the promoter comprises a promoter functional in a plant or plant cell, and wherein the transcription unit encodes a fusion protein, wherein the fusion protein comprises (1) a viral protein, (2) a protein of interest, and (3) an autoproteolytic peptide

comprising no more than 20 amino acids, wherein (3) is fused between (1) and (2). Claim 19 is drawn to a recombinant virus comprising a recombinant viral nucleic acid of claim 17 (e.g., comprising the polynucleotide according to claim 1, encoding a fusion protein in which the autoproteolytic peptide is fused to the N-terminus of the viral protein βb, which is fused to the N-terminus of the autoproteolytic peptide), where the recombinant virus is capable of systemic expression of the fusion protein. Claim 20 is drawn to a plant or a plant cell infected with the recombinant virus of claim 19. Claims 24 and 26 are drawn to plant cells or plants, respectively, that are infected with a recombinant virus according to claim 23 (e.g., comprising the recombinant viral nucleic acid comprising the polynucleotide according to claim 1).

The Office Action correctly states that Donnelly does not teach plant viruses or monocot plants; rather, Donnelly is directed towards animal virus sequences disposed within plasmids for expression in prokaryotes. As such, polynucleotides with promoters functional in plant cells are not considered. Choi is alleged to teach a single stranded plant virus RNA based upon wheat streak mosaic virus, as well as infected plant cells and monocot plant cells/plants expressing foreign genes. At page 548, column 2 of Choi, reference is made to "the development of a WSM-based gene vector capable of systemic expression of foreign genes in wheat and other cereals." While plant virus vectors are employed, Choi does not teach the use of an autoproteolytic peptide having no more than 20 amino acids. The plant virus vectors described in Choi employ multiple proteases for cleavage of the polyprotein, including nuclear inclusion a protease (NIa). The potyviral protease NIa is a cysteine protease of the C4 family having a molecular weight of approximately 48-49kD, and does not fit into the category of autoproteolytic peptides having no more than 20 amino acids. Since the cited references, alone or in combination, do not teach the limitations of the claimed invention, the first requirement for proving a *prima facia* case for obviousness has not been met.

The Office suggests that one of skill in the art would be motivated to combine the two references, e.g., the second requirement for proving obviousness. Applicants disagree, and submit that there is no motivation to combine Donnelly with Choi. As a first point, Choi was allegedly successful in developing a WSMV-based gene vector capable of systemic infection of foreign genes (see page 548, column 2 above "Results" section). Thus, Choi does not provide any motivation to develop a further gene vector. The Donnelly reference is directed toward "cleavage activities of aphthovirus and cardiovirus 2A proteins," and the plasmid constructs described therein were

prepared for the purpose of comparing the cleavage site properties between these two animal virus-derive proteases. There is no motivation in Donnelly to combine these protease sequences into a vector capable of expression in a plant cell. Since the Office has not provided motivation based upon the prior art (and *not* derived from the Applicants own disclosure) to combine the cited references, Applicants submit that the second requirement for proving a *prima facia* case of obviousness has not been met.

Finally, even if one could find reason to combine these disparate references, there is no reasonable expectation of success upon combination of these references. The Office Action suggests that "one of skill in the art would have been motivated at the time of invention to substitute for the FMDV of Donnelly the virus of Choi with a reasonable expectation of success." The Choi reference relates to plant viruses, and the Donnelly reference is directed toward animal virus components. Given the differences in plant and animal expression systems, as well as the inherent difficulties in expressing foreign genes using viral vectors, there is no reason to assume that an animal virus-derived sequence will be functional in a fusion protein encoded by a polynucleotide under expression of a promoter functional in plants. Applicants' own disclosure *must not* be used (in hindsight) to provide either the teaching or suggestion to combine or the expectation of success. Applicants also note that substitution of the Choi viral vector for the foot and mouth disease sequences of Donnelly, as directed by the Office Action, would still provide a prokaryotic expression vector based on an E.coli T7 virus construct (containing the Choi vector sequences while removing the FMDV-encoded autoproteolytic sequence of interest in Donnelly), and not a polynucleotide or viral vector comprising a promoter operatively linked to a transcriptional unit, wherein the promoter comprises a promoter functional in a plant or plant cell, and wherein the transcription unit encodes a fusion protein, wherein the fusion protein comprises (1) a viral protein, (2) a protein of interest, and (3) an autoproteolytic peptide comprising no more than 20 amino acids, wherein (3) is fused between (1) and (2). Applicants submit that the third requirement for proving a *prima facia* case of obviousness, a reasonable expectation of success, has not been met.

Thus, Applicants maintain that the claimed invention is not rendered unpatentable over Donnelly in further view of Choi, because the cited references in combination do not teach the limitations of the claims, there is no motivation to combine the cited references, and there would not have been a reasonable expectation of successfully combining these references to achieve the results of the present invention. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants respectfully submit that pending claims are novel and nonobvious over the art. The foregoing amendments are believed to place the application in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. **In the event that any issues of substance are perceived to remain, Applicants request that the Examiner contact the undersigned to arrange for a telephonic interview, prior to preparation of any additional Office Action.**

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Respectfully submitted,

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